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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,408	04/25/2006	Francesco Cilurzo	207,565	1408

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EXAMINER	
SUTTON, DARRYL C	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/577,408	CILURZO ET AL.	
	Examiner	Art Unit	
	DARRYL C. SUTTON	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *6-11,18-20,25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,12-17 and 21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/31/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group II, claims 1-17 and 21-24, and species election of (a) ondansetron in the reply filed on 10/27/2009 is acknowledged. The elected species ondansetron is an anti-emetic active and does not have a food use or topical activity. Accordingly, claims 6-11, 18-20 and 25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 recites the limitation "therapeutic use" in line 2 of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claims 12 and 13 recite the limitation "active principle" in line 2 of the claim. There is insufficient antecedent basis for this limitation in the claim.

The term "essentially systemic activity" in claims 12 and 13 is a relative term which renders the claims indefinite. The term "essentially systemic activity" is not

defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. One of ordinary skill would not be able to ascertain how much systemic activity the active would need to possess to qualify as "essentially" systemic.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 5, 12-14, 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falkenhausen et al. (WO 2002/02085); US 2004/0028732 is being used as translation guide.

Falkenhausen et al. teach a rapidly disintegratable dosage form which is sheet-like comprised of a matrix which comprises a water soluble polymer and at least one active ingredient (Abstract, [0001]). The matrix comprises a water soluble polymer such as polysaccharides, pullulan, gel-forming proteins and protein hydrolysates [0017]. The dosage form has a reduced tendency to stick or adhere to the oral mucosa which provided improves mouthfeel [0006] and [0008]. The thickness of the dosage forms have a lower limit of 50 µm [0019]. Suitable active ingredients are therapeutically active compounds such as ondansetron, in amounts of up to 50 mg [0020]. Other agents include peppermint oil [0023]. Suitable excipients include microcrystalline cellulose and carbohydrates which result in a film with a sweet taste, i.e. a sweetener, such as maltodextrin [0027]-[0028]. To improve the esthetic properties and in order to reduce the fragility or brittleness, glycerol or propylene glycol may be added [0030]. First a dispersion comprising at least one film-forming polymer and at least one active ingredient is prepared. The composition is spread as a film or layer on a suitable substrate and is then dried [0033]. Water is used as a solvent to prepare the dispersion which is heated [0041]. It is also possible to produce the dosage forms starting with a polymer melt of the matrix polymer [0037], i.e. the polymer, solvent, active and excipients are combined and then heated. The melt is then spread or extruded onto suitable substrate and left there to cool and solidify. Processing from the melt is

unsuitable if the intended active ingredient is instable or volatile at the melting point of the polymer melt [0038].

Falkenhausen et al. do not teach a specific embodiment of a film comprised of maltodextrin, a plasticizer and ondansetron.

The specific combination of features claimed is disclosed within the broad generic ranges taught by the reference but such "picking and choosing" within several variables does not necessarily give rise to anticipation. Corning Glass Works v. Sumitomo Elec., 868 F.2d 1251, 1262 (Fed. Circ. 1989). Where, as here, the reference does not provide any motivation to select this specific combination of variables: filmogenic substance, excipients, active ingredient, and solvent, anticipation cannot be found.

That being said, however, it must be remembered that "[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious". KSR v. Teleflex, 127 S,Ct. 1727, 1740 (2007)(quoting Sakraida v. A.G. Pro, 425 U.S. 273, 282 (1976)). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious", the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (Id.). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of

ordinary skill in the art would employ." KSR v. Teleflex, 127 S.Ct. 1727, 1741 (2007). The Court emphasized that "[a] person of ordinary skill is… a person of ordinary creativity, not an automaton." Id. at 1742.

Consistent with this reasoning, it would have obvious to have selected various combinations of various disclosed ingredients polysaccharide; microcrystalline cellulose; glycerol or propylene glycol; peppermint oil; water; and maltodextrin from within a prior art disclosure, to arrive compositions "yielding no more than one would expect from such an arrangement".

Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falkenhausen et al. as applied to claims 1, 4, 5, 12-14, 16 and 17 above, and further in view of Kasper et al. (US 4,222,973).

Falkenhausen et al. is discussed *supra*.

Falkenhausen et al. do not teach a method step comprised of heating to the specific temperatures or of tolling onto a silicone paper.

Kasper et al. teach that release papers have long been used for casting films. Conventionally, the papers have been coated with silicon which provides a release layer between the cast surface and the paper, allowing it to be easily removed from the paper (column 1, lines 15-24).

Kasper et al. do not teach a film comprised of maltodextrin.

At the time of the invention, it would have been obvious to use the silicone release papers of Kasper et al. as the substrate onto which the film is spread motivated by the desire to be able to easily remove the film for use or further processing.

At the time of the invention, the therapeutic efficacy of the ondansetron could be optimized thorough routine experimentation by varying the heat at which the dispersion was heated. As cited in Falkenhausen et al., it is not preferable to process the composition at heats which cause instability, i.e. degradation, of the active.

Claims 1-5, 12, 13, 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barnhart et al. (US 2005/0118217).

Barnhart et al. teach disintegratable films containing a mixture of high molecular weight and low molecular weight water soluble components and a pharmaceutically active ingredient. Optionally the films contain a starch component, a glucose component, a filler, a plasticizer and /or humectant (Abstract, [0010]). The films are preferably in the form of a monolayer [0011]. The water soluble component of the film component such as polyvinylpyrrolidone and various other polymers so long as the polymer is water soluble [0018] and [0022]. The water soluble low molecular weight need not be a water soluble polymer, and can be any of the glucose components listed below, in a concentration of about 2% to about 80% based on the total weight of the dried film [0023]. Any pharmaceutical ingredient may be used , whether dissolved or dispersed, such as anti-emetics in amounts of about 2 to 20% [0024]. Maltodextrin having a DE of about 16.5 to about 19.5 are particularly suitable glucose components

[0025]. Plasticizers or humectants, such as polyalcohols, i.e. glycerin, and citric acid esters can be used in amounts from about 3 to 30% to impart flexibility to the films [0028]. Flavors and/or sweeteners are added to the film [0029]. Also any color can be imparted to the film [0030]. Fillers such as microcrystalline cellulose can be used [0032]. The film compositions can be prepared by several methods including combining the components in a solvent that is capable of dissolving them such as a mixture of water and ethanol; after forming a homogeneous solution, the active ingredient and any other optional components are then added [0033]. The active may be dispersed in the solution [0034]. The dispersion is further processed into a film by any one of many casting, drawing, or extruding techniques, such as roll coating onto a release treated paper [0035]. After coating the dispersion onto a support surface the solvent is removed to yield a dry film, which can be removed from the support surface [0036].

Barnhart does not teach a specific embodiment comprised of maltodextrin, plasticizer and active; or the specific amounts of each.

The specific combination of features claimed is disclosed within the broad generic ranges taught by the reference but such "picking and choosing" within several variables does not necessarily give rise to anticipation. Corning Glass Works v. Sumitomo Elec., 868 F.2d 1251, 1262 (Fed. Circ. 1989). Where, as here, the reference does not provide any motivation to select this specific combination of variables: high molecular weight component, low molecular weight component, active ingredient, optional components, and solvent anticipation cannot be found.

That being said, however, it must be remembered that "[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious". KSR v. Teleflex, 127 S,Ct. 1727, 1740 (2007)(quoting Sakraida v. A.G. Pro, 425 U.S. 273, 282 (1976)). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious", the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (Id.). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." KSR v. Teleflex, 127 S.Ct. 1727, 1741 (2007). The Court emphasized that "[a] person of ordinary skill is… a person of ordinary creativity, not an automaton." Id. at 1742.

Consistent with this reasoning, it would have obvious to have selected various combinations of various disclosed ingredients polyvinylpyrrolidone; maltodextrin; anti-emetic; glycerin; sweetener; microcrystalline cellulose; water and a mixture of water and ethanol from within a prior art disclosure, to arrive compositions "yielding no more than one would expect from such an arrangement".

Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barnhart et al. as applied to claims 1-5, 12, 13, 16 and 17 above, and further in view of Levitt et al. (NEJM, 1993).

Barnhart et al. is discussed *supra*.

Barnhart et al. does not teach ondansetron as the active.

Levitt et al. teach that ondansetron is an anti-emetic active (page 1,Title, Background).

Levitt et al. do not teach self-supporting films comprised of ondansetron.

Generally, it is *prima facie* obvious to select a known material for incorporation into a composition, based on its recognized suitability for its intended use. See MPEP 2144.07. Accordingly, it would have been obvious to include the ondansetron of Levitt et al. into the composition of Barnhart et al. as the anti-emetic active.

In regard to claim 15, Barnhart et al. do not teach the specific weight percentages of the components. The prior art does not disclose the exact claimed values, but does overlap: in such instances even a slight overlap in range establishes a *prima facie* case of obviousness. In re Peterson, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003). Barnhart et al. teach from about 2% to 80% of maltodextrin versus from 40 to 80%; from about 3 to 30% of plasticizer versus from 15 to 55%; and from about 2 to 20% of active versus form 0.05 to 30% of the instant claim.

Claims 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barnhart et al. as applied to claims 1-5, 12, 13, 16 and 17 above, and further in view of Kasper et al. (US 4,222,973).

Barnhart et al. is discussed *supra*.

Barnhart et al. does not teach a silicone paper or the heating steps of the instant claims.

Kasper is discussed *supra*.

Kasper et al. does not teach maltodextrin films.

At the time of the invention, it would have been obvious to modify the methods of Barnhart et al. to include the silicon release paper of Kasper et al. as the substrate onto which the film is rolled motivated by the desire to be able to easily remove the film for use or further processing.

It would have been obvious to modify the method to include heating since Barnhart et al. teach that the dispersion is further processed into a film by any one of many casting, drawing, or extruding techniques; and heating is an art recognized method step in casting and drawing techniques, See Falkenhausen *supra*. Further, since Barnhart et al. teach that a homogeneous solution is prepared, heating would assist in the solubilization of the components added to the water and/or ethanol solvent. The efficacy of the active, i.e. anti-emetic activity, could be optimized through routine experimentation by varying the temperature at which the composition is heated to maximize the formation of a homogeneous solution while preventing degradation of the suspended active, i.e. ondansetron, due to heat.

All claims are rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Darryl C. Sutton whose telephone number is (571)270-3286. The examiner can normally be reached on M-Th from 7:30AM-5:00PM EST and on Fr from 7:30AM-4:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached at (571)272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Darryl C Sutton/
Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612